

REMARKS

By this amendment, applicants have canceled claims 1 - 10, 13, 14, 17 and 18 without prejudice or disclaimer and have amended claim 11 to include therein the limitations previously recited in dependent claims 13, 14 and 18 and also to include an upper limit of the acetylation degree disclosed at page 13, lines 6 - 8 of applicants' specification. Applicants have also amended claims 15 and 16 to depend from and be consistent with claim 11. Claim 19 has been amended to recite that the oxidized polyglycosamine derivative is selected from the group consisting of chitin, chitosan, polygalactosamine, and derivatives thereof.

In view of the foregoing amendments to the claims, it is submitted all of the claims now in the application comply with the requirements of 35 USC 112, second paragraph. Therefore, reconsideration and withdrawal of the rejection of claims 1 - 18 under 35 USC 112, second paragraph, are requested.

In view of the cancellation of claims 1 - 10, 13, 14, 17 and 18, the rejection of claims 1 - 3, 5, 7 and 8 under 35 USC 102(a) as being anticipated by Bragd et al, the rejection of claims 1, 2, 5, 6 and 8 under 35 USC 102(b) as being anticipated by Besemer et al "with inherency supported by Merck," the rejection of claims 1 - 3, 5 and 8 - 10 under 35 USC 102(b) as being anticipated by Besemer et al, the rejection of claims 9 and 10 under 35 USC 102(b) as being anticipated by Szu et al and the rejection of claims 13 and 14 under 35 USC 103(a) as being unpatentable over Muzzarelli et al in view of Cardinal et al are moot.

The rejection of claims 1, 2, 5, 8, 11, 12, 15 and 16 under 35 USC 102(b) as being anticipated by Muzzarelli et al is noted. However, in view of the cancellation of

claims 1 - 10, 13, 14, 17 and 18 and the amendments to claim 11, incorporating therein the limitations previously recited in dependent claims 13, 14 and 18, and since claims 13, 14 and 18 were not rejected as being anticipated by Muzzarelli et al, this rejection is also moot.

The rejection of claims 1, 2, 5, 8 - 12, 15 and 16 under 35 USC 102(b) as being anticipated by Chang et al is noted. However, in view of the cancellation of claims 1 - 10, 13, 14, 17 and 18 and the amendments to claim 11 incorporating therein the limitations previously recited in dependent claims 13, 14 and 18, and since claims 13, 14 and 18 were not rejected as being anticipated by Chang et al, this rejection is also moot.

The rejection of claims 11, 12, 16 and 18 under 35 USC 103(a) as being unpatentable over Bragd in view of Muzzarelli et al is noted. However, in view of the foregoing amendments to claim 11, incorporating therein the limitations of claims 13, 14 and 18, and since claims 13 and 14 were not rejected over the combination of Bragd and Muzzarelli et al, this rejection is also moot.

Claims 1, 2, 4, 5, and 8 - 16 stand rejected under 35 USC 102(b) as allegedly being anticipated by Isogai et al with the Cardinal et al patent "to support inherency." Applicants traverse this rejection and request reconsideration thereof.

The present invention relates to a process for producing an oxidized polyglycosamine derivative and to an oxidized polyclycosamine derivative. According to the process of the present invention, as set forth in independent claim 11, the process comprises pretreating by controlling an acetylation degree of an amino group of a polyglycosamine to 0.3 to 0.8 to enhance a water solubility thereof, and oxidizing the

pretreated polyglycosamine with hypochlorous acid or a salt thereof in the presence of a nitroxyl compound and in the absence of a bromine, a bromide, an iodine or an iodide.

The Isogai et al article discloses oxidation of various celluloses, chitan and chitosan using TEMPO, NaBr and NaClO. Thus, this document does not disclose oxidizing polyglycosamine in the absence of a bromine, a bromide, iodine or an iodide. Moreover, this document does not disclose pretreating the polyglycosamine by controlling an acetylation degree of an amino group thereof to 0.3 to 0.8 to enhance a water solubility thereof.

The Examiner relies on the Cardinal et al patent for its teachings that chitosan is a common name for the deacetylated form of chitan and that, on deacetylation, chitan becomes soluble in dilute organic acid. However, the Cardinal patent does not remedy one of the basic deficiencies noted above with Isogai et al, i.e., that Isogai et al does not suggest oxidizing a pretreated polyglycosamine in the absence of bromine, a bromide, iodine or an iodide. Accordingly, the presently claimed invention is patentable of Isogai and Cardinal et al.

Claim 19 stands rejected under 35 USC 102(b) as allegedly being anticipated by United States Patent No. 5,925,626 to della Valle et al. Applicants traverse this rejection and request reconsideration thereof.

Claim 19 is directed by an oxidized polyglycosamine derivative selected from the group consisting of chitin, chitosan, polyglycosamine and derivatives thereof having a molecular weight of 100,000 or more, in which 40% or more of primary alcohol groups of repeating units are oxidized into carboxyl groups.

The della Valle et al patent discloses that two pharmaceutically useful fractions of

hyaluronic acid are obtained comprising a first fraction with a molecular weight between 50,00 and 100,000, which is useful for wound healing, and a second fraction having a molecular weight between 500,000 and 730,000 which is useful for intraocular and for intraarticular injections. However, this patent does not disclose an oxidized polyglycosamine derivative selected from the group consisting of chitin, chitosan, polygalactosamine and derivatives thereof having a molecular weight of 100,000 or more in which 40% or more primary alcohol groups of repeating units or oxidized into carboxyl groups. Accordingly, claim 19 is patentable over della Valla et al.

Claims 1, 2, 5, 6 and 8 - 17 stand rejected under 35 USC 103(a) as being unpatentable over International Publication No. 95/07303 to Besemer et al and Isogai et al. Applicants traverse this rejection and request reconsideration thereof.

Besemer '303 discloses a method for oxidizing carbohydrates having a primary hydroxyl group by treatment with hypohalite in the presence of a catalytic amount of ditertiary-alkyl nitroxyl. It is disclosed that the hypohalite used can be hypochlorite or a hypobromite which is preferably obtained in the reaction medium from hypochlorite and bromide. However, this document does not disclose controlling an acetylation degree of an amino group of a polyglycosamine to 0.3 to 0.8 to enhance a water solubility thereof before oxidizing it. While the Examiner relies on the Isogai reference for teaching that the degree of polymerization of the oxidization product is dependent on the amount of bromide used in the reaction, it is noted that the oxidization step according to the present invention is carried out in the absence of bromine, a bromide, iodine or an iodide. Accordingly, the presently claimed invention is patentable over the proposed combination of Besemer '303 and Isogai et al.

Claim 19 stands rejected under 35 USC 103(a) as being unpatentable over Chang et al in view of Muzzarelli et al. Applicants traverse this rejection and request reconsideration thereof.

The Chang et al article discloses oxidization of primary alcohol groups of ten polysaccharides to carboxyl groups using TEMPO. As recognized by the Examiner, the Chang et al article does not disclose the molecular weight of the final products.

The Muzzarelli et al article discloses that oxychitin can be obtained from chitin by regioselective oxidation of the primary alcohol group carboxylate and that oxychitin can be reacted with chitosan to produce microcapsules by polyelectrolyte coacervation. While this document discloses chitosan salts having molecular weights greater than 100,000, it is submitted nothing in Chang et al and Muzzarelli et al would have suggested the oxidized polyglycosamine derivative presently claimed which has a molecular weight of 100,000 or more and in which 40% or more of the primary alcohol groups of repeating units are oxidized into carboxyl groups.

It is noted that in both Chang et al and Muzzarelli et al, the oxidation is conducted in the presence of sodium bromide. Applicants have found, however, in order to prevent the cleavage of molecular chains during oxidation, sodium bromide should not be present within the reaction system. Noting that both Chang and Muzzarelli et al carry out oxidation in the presence of sodium bromide, it is submitted it cannot be reasonably expected, as alleged by the Examiner, that the teachings of Chang and Muzzarelli would suggest an oxidized polyglycosamine derivative selected from the group consisting of chitin, chitosan, polygalactosamine, and derivatives thereof having a molecular weight of 100,000 or more, in which 40% or more are primary alcohol groups

of repeating units are oxidized into carboxyl groups. Accordingly, claim 19 is patentable over the proposed combination of references.

In view of the foregoing amendments and remarks, favorable reconsideration and allowance of all of the claims now in the application are requested.

To the extent necessary, applicants petition for an extension of time under 37 CFR 1.136. Please charge any shortage in the fees due in connection with the filing of this paper, including extension of time fees, to the deposit account of Antonelli, Terry, Stout & Kraus, LLP, Deposit Account No. 01-2135 (Case: 396.41133X00), and please credit any excess fees to such deposit account.

Respectfully submitted,

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